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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,550	07/19/2005	Bruno Bujoli	032013-102	1306

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EXAMINER	
SHIAO, REI TSANG	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
04/11/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/506,550	BUJOLI ET AL.	
	Examiner	Art Unit	
	Rei-tsang Shiao, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/03/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign application:

FRANCE 02/02707 with a filing date 03/04/2002.

2. Claims 1-18 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement, filed on September 03, 2004 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Responses to Election/Restriction

4. Applicant's election with traverse of election of Group II claims 1-18, in part, in the reply filed on January 10, 2008 is acknowledged. Election of a species alendronate (i.e., R^1 = OH, R^2=$(CH_2)_3$-NH_2) is also acknowledged. The traversal is on the grounds that applicants respectfully submit that all of the compounds of claim 1 have both a common property and common activity, and M.P.E.P. 1850 (III)(B) is cited. This is found not persuasive, and the reasons are given *infra*.

Claims 1-18 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-18, in part, drawn to compounds/composition of the formula of claim 1, when the variable R^2 represents an alkyl radical bearing an aromatic substituted not comprising at least one N atom thereof, and their processes of making.

The claims 1-18 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element

qualifying as the special technical feature that defines a contribution over the prior art, see Poss's US 5,208,234. Bright et al. discloses similar imidazole compounds/ compositions and their salts as the instant invention, see formula (I) in column 1. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

(1) A product and a process specially adapted for the manufacture of said product', or

(2) A product and a process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

> the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-II are drawn to various products and processes of making do not contain a common technical feature or structure of claims 1-18, and do not define a contribution over the prior art, i.e., compounds/compositions of Poss's US 5,208,234. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. Claims 1-18, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 1-18, in part, not embraced in above elected subject matter, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising compounds of the formula of claim 1 , does not reasonably provide enablement for the intent methods of

use for the instant compositions, see claim 16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 16-18 are drawn a composition comprising compounds of the formula of claim 1 with intent methods of use for treating osteoporosis.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face. Poss's US 5,208,234 discloses similar compounds for treating hypertension, see lines 56-60 of column 12.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming a composition comprising compounds of the formula of claim 1 with intent methods of use for treating osteoporosis. As such, the specification fails to enable the skilled artisan to use the compositions of claims effective to "treating osteoporosis " .

In addition, there is no established correlation between *in vitro* or in *vivo* activity and accomplishing treatment of "treating osteoporosis", and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the compositions

comprising compounds of the formula of claim 1 since there is no description of an actual method wherein "treating osteoporosis" in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds/compositions of claims 16-18 due to the unpredictability of the "treating osteoporosis". The "treating osteoporosis" is known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of exemplary tests of modified calcium phosphate of rabbit bone cells, *in vitro*, see Example 4 of pages 11-12 of the specification. There are no *in vivo* working examples present for the treatment of osteoporosis by the administration of the instant invention.

The breadth of the claims

The breadth of the claims is the instant compositions/compounds with intent methods of use effective to "treating osteoporosis". Moreover, there is no reasonable basis for assuming the instant compositions/compounds of the formula of claim 1 embraced by the claims will share the same physiological properties.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in

the art would need to determine what “treating osteoporosis” without limitation would be benefited (i.e., treated) by the administration of the instant compositions/compounds of the formula of claim 1 of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment of a disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims for the “treating osteoporosis”.

As a result necessitating one of skill to perform an exhaustive search for which “treating osteoporosis”, can be treated by what pharmaceutical compositions/ compounds of the instant claims in order to practice the claimed invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds in regards to the treatment of the many diseases resulting from “treating osteoporosis”, one having

ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by deleting the preamble "that may be used by injection ….osteoclast activity" of claim 16 would obviate the rejection.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-18 are rejected under 35 U.S.C. 102(b) as being anticipated by (1) Bikhman et al. CAS: 94:1762; (2) Kostromina et al. CAS: 136: 75305; (3) Cohen et al. CAS: 129:49620; or (4) Zaher et al. CAS: 136:163487;

Applicants claim a phosphocalcic compound of the formula, i.e.,

$Ca_{(10-a)}(Mg, K, Na)_b(PO\ 4)_{6-c}\ (HPO_4, CO_3)d(OH)_{2-e}(F, Cl, CO_3)_f$ [(OA)(OE)P(O)-CR^1-R^2-P(O)(OA)(OE)]g, and their compositions and processes of making.

6.1 Bikhman et al. disclose a phosphocalcic compound, see RN: 75885-40-4, it clearly anticipates the instant compound of the above formula, wherein the variable R^1 represents OH, and the variable R^2 represents an alkyl radical (i.e., methyl).

6.2 Kostromina et al. disclose a phosphocalcic compound, see RN: 383417-21-8, it clearly anticipates the instant compound of the above formula, wherein the variable R^1 represents OH, and the variable R^2 represents an alkyl radical (i.e., methyl).

6.3 Cohen et al. disclose four phosphocalcic compounds, see RN: 172913-38-1, 203264-12-4, 40391-99-9 or 66376-36-1, they clearly anticipate the instant compound of the above formula, wherein the variable R^1 represents hydrogen or OH, and the variable R^2 represents aminoalkyl or an alkyl radical (i.e., methyl) substituted with aromatic substitutent comprising two N atoms (i.e., pyrimidine or imidazole).

6.4 Zaher et al. disclose a phosphocalcic compound, see RN: 91357-22-1, it clearly anticipates the instant compound of the above formula, wherein the variable R^1 represents OH, and the variable R^2 represents aminoalkyl.

Dependent claims 2-18 are also rejected along with claim 1 under 35 U.S.C. 102(b).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of Khairoun et al. US 7,351,280. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim a composition comprising phosphocalcic compounds (i.e., BCP, CDA or β-TCP).

Khairoun et al. claim a composition comprising BCP or β-TCP, see claim 1.

The difference between the instant claims and Khairoun et al. is that Khairoun et al. '280 is silent on the instant named phosphocalcic compounds or the formula of claim 1. Khairoun et al. inherently overlap with the scope of the instant invention.

One having ordinary skill in the art would find the instant claims 16-18 prima facie obvious **because** one would be motivated to employ the processes of Khairoun et al. to obtain the instant compositions, wherein phosphocalcic compounds are selected from BCP, CDA or β-TCP.

The motivation to obtain the claimed processes derives from known Khairoun et al. compositions would possess similar activity (i.e., treating osteoporosis) to that which is claimed in the reference.

Claim Objections

8. Claims 1-18 are objected to as containing non-elected subject matter, i.e., comprising at least one N atom of the variable R^2, pyridyl, imidazolyl group, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on pages 2-3, *supra*.

9. Claims 15 is objected to because of the following informalities: a term "or" is missing after the phrase "one N atom", see page 17, line 8.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

Rei-tsang Shiao, Ph.D.
Primary Patent Examiner
Art Unit 1626

April 02, 2008